REMARKS

Claims 1-11 have been canceled without prejudice for future prosecutions. New claims 12-27 have been added. Claims 12-27 are pending in this application.

I. The Section 112 Rejection

The Examiner rejected claims 1 to 3 and 6 to 9 under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure. This rejection is respectfully traversed. Applicant submits that new claims 12-27 are fully enabled by the specification.

New claim 12 covers an isolated, purified, enriched or recombinant nucleic acid encoding SEQ ID NO:2. The Examiner stated on page 3 of the office action that "the disclosure is enabling **only** for claims to a nucleic acid encoding a human PPARγ having the entire amino acid sequence presented in SEQ ID NO:2."

However, the specification describes that a human PPARγ polypeptide may also start from the second methione (amino acid residue 18) or the third methione (amino acid residue 20) of SEQ ID NO:2 (e.g. page 51 of the specification). Therefore,

applicant submits that the disclosure is also enabling for claims 13 and 14 directed to isolated, purified, enriched or recombinant nucleic acid encoding amino acid residue 18 to 494 or 20 to 494 of SEQ ID NO:2.

In addition, the disclosure on pages 7-9 and 51 of the specification describes nucleic acids encoding at least 20 contiguous amino acids of a human PPARγ polypeptide. Therefore claims to isolated, purified, enriched, or recombinant nucleic acid containing no less than 60 contiguous nucleotides selected from nucleotide 157 (i.e. the beginning of the first start codon) to 1641 of SEQ. ID. NO. 1 are fully supported by the specification. So are claims to isolated, purified, enriched, or recombinant nucleic acid containing no less than 60 contiguous nucleotides selected from the second or third ATG start codon to the stop codon of human PPARγ gene in SEQ ID NO:1.

The above claimed nucleic acids containing no less than 60 contiguous nucleotides from the coding region of human PPARγ may be used as probes for diagnosis or as primers for cloning.

Applicant submits that new claims 12-27 are significantly different from claim 7 of Amgen, which states:

> 7. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding polypeptide having an amino acid sequence sufficiently duplicative of that of erythropoietin to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells, and to increase hemoglobin synthesis or iron uptake.

Claim 7 of Amgen claims DNA encoding polypeptide of yet **undefined** sequence. In this application, however, both the amino acid sequence of human PPARγ protein and the nucleotide sequence of human PPARγ gene are disclosed. Therefore, the rationale for rejecting claim 7 of Amgen does not apply in this case.

II. The Section 103 Rejection

The Examiner rejected claims 1-3 and 6-9 under 35 U.S.C. § 103 as being obvious over Chen et al. in view of Sher et al. This rejection is respectfully traversed.

A. Prior art cited by the Examiner

Chen et al. described identifying mNUCI and mPPARγ from mouse cDNA libraries. The nucleotide sequence and amino acid sequence of mPPARγ are disclosed in Chen et al.

Sher et al. described cloning human PPARα from a human liver cDNA library using two mouse PPARα primers.

Neither Chen et al. nor Sher et al. described the existence of a human PPARγ gene, let alone the nucleotide sequence of SEQ ID NO:1 or the amino acid sequence of SEQ ID NO:2.

The Examiner argued that Sher et al. has shown that the existence of a murine PPAR gene was predictive of the existence of a corresponding human PPAR gene, and it would have been obvious for an artisan to screen a human cDNA library with the murine PPARγ cDNA for a human PPARγ gene.

B. Burden of proof by the Examiner

> The examiner bears the burden of establishing a *prima facie* case of obviousness. Only if this burden is met does the burden of coming forward with rebuttal argument or evidence shift to the applicant. When the references cited by the examiner fail to establish a

> *prima facie* case of obviousness, the rejection is improper and will be overturned. (citations omitted) In re Deuel, 34 USPQ2d 1210, 1214 (Fed. Cir. 1995).

As discussed below, the references cited by the examiner fail to establish a *prima facie* case of obviousness.

C. The difference between the prior art and the claimed invention

To determine patentability under § 103, it is necessary to determine the difference between the prior art and the claimed invention, and then determine if the differences are such that the subject matter sought to be patented as a whole would have been obvious to a person of skill in the art at the time the invention was made. The issue is not whether the differences between the prior art and the claimed invention would have been obvious, but whether the subject matter as a whole would have been obvious. Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966).

When evaluating a claim for determining obviousness, all limitations of the claim must be evaluated. The invention must be reviewed as a whole. In re Gulack, 217 USPQ 401 (Fed. Cir. 1983).

The claimed invention covers human PPARγ polypeptides of specific and identified amino acid sequences and nucleic acids encoding the human PPARγ polypeptides. This application does not claim a method of predicting or obtaining a cDNA clone of human PPARγ.

The difference between claims 12-27 and the prior art thus lies with the subject matter of this invention: nucleic acids encoding human PPARγ polypeptides, which are not described by Chen et al. or Sher et al.

D. Obviousness inquiry for a product should focus exclusively on the product itself, and not on the method for making it.

It is improper to reject claims to molecules based on the alleged obviousness of a method of making the molecules. In re Deuel, 34 USPQ2d 1210, 1214 (Fed. Cir. 1995).

Because pending claims 12-27 are about nucleic acids, a *prima facie* case of unpatentability requires that the prior art describe or suggest the claimed nucleic acids to a person of ordinary skill in the art. In view of the mouse PPARγ DNA sequence in Chen et al. the question becomes "whether the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention." In re Deuel at 1214.

There is no inkling in Chen et al. or Sher et al. as to what modifications to make to the mouse PPARγ DNA to change it into a human PPARγ DNA.

E. What cannot be contemplated or conceived cannot be obvious.

One could not have conceived the subject matter of claims 12-27 based on the teachings in the cited prior art because, until the claimed molecules were actually isolated and purified, it would have been highly unlikely for one of ordinary skill in the art to contemplate what was ultimately obtained,

e.g. SEQ ID NO:1. "What cannot be contemplated or conceived cannot be obvious." In re Deuel at 1215.

"Conception of a substance claimed *per se* without reference to a process requires conception of its structure, name, formula, or definitive chemical or physical properties." Fiers v. Sugano, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). "[W]hen an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated." Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).

Like the claims in Amgen and Fiers, claims 12-27 were not conceived until human PPARγ was actually cloned or sequenced.

F. "Obvious to try" does not constitute obviousness.

The Examiner's theory that one might have been motivated to try to do what the applicant in fact accomplished amounts to speculation and an impermissible hindsight reconstruction of the claimed invention. It ignores the fact

that claims 12-27 are limited to specific nucleic acid compounds, and any motivation that existed was a general one, to try to obtain a gene that was yet undefined and may have constituted many forms. "A general motivation to search for some gene that may or may not exist does not necessarily make obvious a specifically-defined gene that is subsequently obtained as a result of that search." In re Deuel at 1215.

The case for obviousness here is even weaker than Deuel. Unlike In re Deuel, where the existence of a gene was known because the protein had been isolated, it was not certain whether any human PPARγ gene exists or not before this invention because human PPARγ protein had not been isolated and identified.

G. A compound can be defined by its process of preparation only after it has been prepared.

"The PTO's focus on known methods for potentially isolating the claimed DNA molecules is also misplaced because the claims at issue define compounds, not methods. See In re Bell, 991 F.2d 781, 785, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993)." In re Deuel at 1215.

"[T]he existence of a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious, in the absence of other prior art that suggests the claimed DNAs." In re Deuel at 1215.

> Thus, even if, as the examiner stated, the existence of general cloning techniques, coupled with knowledge of a protein's structure, might have provided motivation to prepare a cDNA or made it obvious to prepare a cDNA, that does not necessarily make obvious a particular claimed cDNA. "Obvious to try" has long been held not to constitute obviousness. In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680-81 (Fed. Cir. 1988). A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out.

In re Deuel at 1216.

> The fact that one can conceive a general process in advance for preparing an undefined compound does not mean that a claimed specific compound was precisely envisioned and therefore obvious. A substance may indeed be defined by its process of preparation. That occurs, however, when it has already been prepared by that process and one therefore knows that the result of that process is the stated compound. The process is part of the definition of the compound. But that is not possible in advance, especially when the hypothetical process is only a general one. Thus, a conceived method of preparing some undefined DNA does not define it with the precision necessary to render it obvious over the protein it encodes.

In re Deuel at 1216.

For the above stated reasons, it is respectfully submitted that Chen et al. and Sher et al. do not provide a *prima facie* case of obviousness.

Accordingly, the claims are now in condition for allowance and a notice to that effect is respectfully requested. If there is any fee due in connection with this response, please charge Deposit Account No. 12-2475 for the appropriate amount.

Respectfully submitted,

LYON & LYON

By: _____
Anthony C. Chen
Registration No. 38,673

LYON & LYON
First Interstate World Center
633 West Fifth Street, Suite 4700
Los Angeles, CA 90071-2066
(213) 489-1600